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Re: New Prostate Cancer Grading System Predicts Long-term Survival Following Surgery for Gleason Score 8–10 Prostate Cancer

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We read with interest the article by Ham et al., which investigates whether dividing Gleason score (GS) 8-10 disease into GS 8 and GS 9-10 provides prognostic information regarding mortality (1). We sought to validate their findings of increased hazards in GS 9-10 compared to GS 8 across other prostate cancer (PC) cohorts with long-term follow-up.

We leveraged data from men of the Health Professionals Follow-up Study and the Physicians' Health Study who were treated by radical prostatectomy (RP) over the period 1983-2009. Of 1,395 men, 279 (20%) scored as GS 8-10. In the GS 8 group (n=108), 18 lethal or metastatic events were observed over a median of 10.2 years follow-up. In the GS 9-10 group (n=171), 37 events were observed over a median of 9.2 years follow-up. The hazard ratio (HR) comparing GS 9-10 to GS 8 was 1.34 (95% CI: 0.74-2.36; p=0.31). The association was similar when adjusted for pathologic stage and age, with HR 1.39 (95% CI: 0.71-2.71). Analogous results emerged from 545 men who underwent RP over the years 1987-2001 at the Mayo clinic (2). Among 211 men with GS 8-10, the odds ratio for lethal or metastatic disease comparing GS 9-10 to GS 8 was 1.21 (95% CI: 1.06-1.39; p=0.01).

Taken together, our analyses suggest that, while the trend of higher mortality in the GS 9-10 compared to GS 8 persists, the prostate cancer-specific HR may be less than the estimate derived from the Johns Hopkins cohort, 2.38 (95% CI: 1.74-3.28). Discrepancies in our point estimates compared to those of Johns Hopkins may arise because of several reasons. First, approximately

8.9% of all men in the Johns Hopkins cohort (2006 to 2016) suffered from GS 8-10 (3). However in the current study only 1047 men which represent only 4.3% were included in the final analysis. Therefore around 1100 (4.6%) men were excluded because “incomplete clinicopathologic or follow-up data”, or a “history of neoadjuvant treatment”. Second, in our and the Mayo cohort but not in the Johns Hopkins cohorts, all RP specimens were rereviewed by study pathologists to assign standardized GS. Third, the median follow-up is distinct between the Johns Hopkins cohort (4 years), our cohort (10 years) and the mayo cohort (17 years). To summarize, we assume certain patient selection in the study by Ham et al. which may led to the observed HR.

More broadly, an elevated HR alone as a measure of prognostic accuracy may be incongruous with clinical utility. Specifically, it is possible for markers to have a large effect on the hazard of death, yet exhibit poor performance discriminating those patients who have lethal cancers from those that do not (4). The latter goal is of elevated importance in clinical decision making, and future analyses that explore the benefit of GS subdivisions on sensitivity, specificity, and predictive values could help clarify their role. We look forward to such studies and, in the meantime, we commend the authors for their insightful and impactful work in this area to date.

Disclosure/Conflict of Interest: The authors declare no conflicts of interest.

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